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10/810,733	03/26/2004	Qiong Cheng	CL2385USNA	3038

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 08/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,733	CHENG ET AL.	
	Examiner	Art Unit	
	Jae W. Lee	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-5,7-14,16 and 20-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,15 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date /.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application status

Claims 1-35 are pending in this application.

The applicant's representative, Neil Feltham, was informed of the restriction requirement on 08/03/2006 over the telephone and he elected Group I and SEQ ID NO 20., and claims 1-5, 7-14, 16, and 20-35 are withdrawn from further consideration on the merits as directed to non-elected claims.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3, 6-19, 34, and 35, drawn to an isolated nucleic acid molecule encoding a carotenoid biosynthetic pathway enzyme, classified in class 536, subclass 23.1.

II. Claims 4, and 5, drawn to a polypeptide, classified in class 435, subclass 183.

III. Claims 20-27, drawn to a method of producing carotenoid compounds, classified in class 435, subclass 67.

IV. Claims 28-32, drawn to a method of regulating carotenoid biosynthesis in an organism, classified in class 435, subclass 471.

V. Claim 33, drawn to a strain DC413, classified in class 435, subclass 252.3.

For inventions I and II above, restriction to one of the following is further required under 35 USC 121. Therefore, Applicants are required elect one of inventions (A)-(H).

(A) SEQ ID NO. 1, and SEQ ID NO. 2 (crtE)

(B) SEQ ID NO. 3, and SEQ ID NO. 4 (idi)

(C) SEQ ID NO. 5, and SEQ ID NO. 6 (crtX)

(D) SEQ ID NO. 7, and SEQ ID NO. 8 (crtY)

(E) SEQ ID NO. 9, and SEQ ID NO. 10 (crtI)

(F) SEQ ID NO. 11, and SEQ ID NO. 12 (crtB)

(G) SEQ ID NO. 13, and SEQ ID NO. 14 (crtZ)

(H) SEQ ID NO. 20 (crtE, idi, crtX, crtY, crtI, crtB, and crtZ)

The inventions are distinct, each from the other because of the following reasons:

The inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, polypeptides, which are comprised of amino acids that fold into a specific three-dimensional structure, and nucleic acids, which are composed of linear, contiguous purine and pyrimidine units, are structurally distinct molecules. In addition, while a polypeptide of invention II can made by methods using some, but not all, of the nucleic acids that fall within the scope of invention I, it can also be recovered from a natural source using biochemical means. For instance, the polypeptide can be isolated

using affinity chromatography. For these reasons, the inventions I and II are patentably distinct.

Invention I and inventions III, and IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the polynucleotide can be used in a materially different process such as one in which the polynucleotide is used for hybridization or detection methods.

Inventions I and V are unrelated. In the instant case, the nucleic acid molecules are composed of linear, contiguous purine and pyrimidine units. However, Pantoea stewartii strain DC413 is structurally different which is comprised of membranes, cytoplasm, organelles, proteins, carbohydrates, nucleic acids, etc. Further, strain DC413 comprises the 16S rDNA sequence as set forth in SEQ ID NO:18 which represents structurally different nucleotide sequences compared to the nucleotide sequences of invention I (SEQ ID Nos 1, 3, 5, 7, 9, 11, and 13). Therefore, where structural identity is required, such as for hybridization or expression, the different sequences have different effects.

Invention II and inventions III, and IV are unrelated. In the instant case, the polypeptide is not used by these processes, and it may be produced by other methods such as chemical synthesis.

Inventions II and V are unrelated. In the instant case, polypeptides of Invention II, which are comprised of amino acids that fold into a specific three-dimensional structure, are different in their modes of operation, functions, structures and effects from Pantoea stewartii strain DC413 which is comprised of membranes, cytoplasm, organelles, proteins, carbohydrates, nucleic acids, etc.

Inventions III and V are unrelated. In the instant case, the Pantoea stewartii strain DC413 comprising the 16S rDNA sequence as set forth in SEQ ID NO 18 is not used by the method for producing carotenoid compounds wherein the host cell is transformed with nucleic acid molecules of SEQ ID NOs 1, 3, 5, 7, 9 ,11, and 13. Further, strain DC413 of Invention V can be used to as a host cell for heterologous expression of polypeptides instead of being used in the method for production of carotenoid compounds.

Inventions IV and V are unrelated. In the instant case, the Pantoea stewartii strain DC413 comprising the 16S rDNA sequence as set forth in SEQ ID NO 18 is not used by the method for regulating carotenoid biosynthesis wherein the host cell is transformed with nucleic acid molecules of SEQ ID NOs 1, 3, 5, 7, 9 ,11, 13, and 20. Further, the strain DC413 of Invention V can be used to as a host cell for heterologous expression of polypeptides instead of being used in the method for regulating carotenoid biosynthesis in an organism.

Inventions III and IV are directed to related processes. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually

exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the method for *production of carotenoid compounds* has different modes of operation, function, or effect from the method for *regulating carotenoid biosynthesis* in an organism thereby producing different results. For example, the *increase* in producing carotenoid compounds using said method of Invention III is distinct from the *increase or decrease* that may result from regulating carotenoid biosynthesis using said method of Invention IV.

Inventions (A)-(G) are unrelated. In the instant case these inventions represent structurally different nucleotide sequences. Therefore, where structural identity is required, such as for hybridization or expression, the different sequences have different effects.

Because these inventions are distinct for the reasons given above, and the literature and sequence searches required for each of the inventions are not required for another of the inventions thereby presenting a search burden on the Examiner, restriction for examination purposes as indicated is proper. Applicant is required under 35 U.S.C. 121 to elect a single Group, even though this requirement may be traversed. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is

allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Applicant is reminded that upon the cancellation of claims to a non-elected species, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

Election

During a telephone conversation with Mr. Neil Feltham on August 3, 2006, a provisional election was made. The Group I drawn to Claims 1-3, 6-19, 34, and 35, and SEQ ID NO 20 were elected by the Applicant. As a result, Claims, 1-3, 7-14, and 16 drawn to SEQ ID NOs other than SEQ ID NO 20 are withdrawn from further consideration in addition to Claims 4, 5, 20-35 as being a non-elected invention according to 37 CFR 1.142(b). Therefore, Claims 1-5, 7-14, 16, and 20-35 are withdrawn from further consideration and Claims 6, 15, and 17-19 will be examined on the merits. Affirmation of this election must be made by applicant in replying to this Office action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

The first line of the specification states that this application claims the priority of U.S. Provisional application 60/488,183, filed July 17, 2003, and U.S. Provisional application 60/527,083, filed December 03, 2003. The incorporation of these applications by reference is acknowledged.

Information Disclosure Statement

Applicants filing of information disclosures, filed 6/14/2004, is acknowledged. Those references considered have been initialed.

Claim Objections

Claims 6, 18 and 19 are objected to because:

Claim 6 recites "95% identity". The clarity of the claim could to be improved by inserting "sequence" so that the claim reads 95% "sequence" identity.

Claims 18 and 19 depend from a non-elected Claim 16.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6, 15, and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite and confusing in the recitation "... the polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ." It is unclear what is encompassed by the referred to polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ. As an example, although the specification recites, "... "CrtE" refers to a geranylgeranyl pyrophosphate synthetase enzyme encoded by the *crtE* gene ...", it is unclear whether truncations, partial deletions, or fragmentations of the encoded polypeptide can be still called a "crtE polypeptide". It is unclear as to what the boundaries or guidelines are for calling something a "crtE polypeptide" when there could be as much as 5% difference in the encoded polypeptide. In addition, it is not clear as to how much enzymatic activity or what enzymatic activities of the polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ must be retained by the polypeptides to be considered as being encompassed by the referred "polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ."

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 15, and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 6, 15, and 17-19 are directed to an isolated nucleic acid molecule of SEQ ID NO 20 comprising *crtE, idi, crtX, crtY, crtI, crtB,* and *crtZ* genes or an isolated nucleic acid molecule having at least 95% identity to SEQ ID NO 20, wherein said nucleic acid molecule encodes all of the polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ. While Applicants' claim clearly recite a structure, (i.e. 95% identity to SEQ ID NO 20), the specification, however, does not provide a disclosure of any particular structure to function/activity relationship of the said isolated nucleic acid molecule and the encoded polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ. The specification also fails to describe any identification of structural characteristics or properties of isolated nucleic acid molecule of SEQ ID NO 20 or one having 95% identity to SEQ ID NO 20 (see 112 2nd paragraph rejection). Given this lack of additional representative of SEQ ID NO 20 as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 6, 15, and 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule of SEQ ID NO 20 comprising *crtE, idi, crtX, crtY, crtI, crtB,* and *crtZ* genes, does not reasonably provide enablement for any isolated nucleic acid having 95% identity to SEQ ID NO 20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 6, 15, and 17-19 are so broad as to encompass any nucleic acid having a mere 95% identity to SEQ ID NO 20 encoding any polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ (see above 112 2nd paragraph rejection). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acids broadly encompassed by the claims, encoding the polypeptides, crtE, idi, crtX, crtY, crtI, crtB, and crtZ, and variants thereof that are encoded by any nucleic acid having 95% identity to SEQ ID NO 20. The claims rejected under this section of U.S.C. 112, first paragraph, place minor structural and no

functional limitations on the claimed nucleic acids. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and thus nucleic acid sequence while obtaining the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

Although, the Applicants disclose in the specification (lines 24-29 on page 29) that minor nucleic acid substitutions, additions and deletions (such as the substitutions of preferred codons for specific host cell expression) may be made to such a gene cluster without affecting its utility provided that all of the encoded polypeptides are expressed and are enzymatically active. Applicants have not provided guidance to make a majority of the encompassed isolated nucleic acid molecule having at least 95% identity to SEQ ID NO 20, wherein said nucleic acid molecule encodes all of the

polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ. The specification does not support the broad scope of the claims which encompass those nucleic acids which encode any polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ because the specification does not establish: (A) regions of the nucleic acid structure which may be modified without affecting the encoded proteins' functions/activities; (B) the general tolerance of the protein to modification and the extent of such tolerance; (C) a rational and predictable scheme for modifying SEQ ID NO 20 thereby changing amino acid residue of the encoded polypeptides with an expectation of obtaining the desired biological function; and (D) the insufficient guidance in the specification as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions, as many as 456 nucleotides (5% of the SEQ ID NO 20), would be acceptable to retain the desired polypeptide functions/activities and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those nucleic acid molecules.

Claims 17-19 are further rejected under this statute because they are directed to a transformed host selected from green plants. Previous studies demonstrate that the transformation of plants or the gene transfer to plants have been difficult with low success rate (Potrykus, Biotechnology 8(6): 535-542). In this regard, the specification

fails to disclose a representative example of a successful transformation of a green plant host with the nucleic acid molecule of SEQ ID NO 20. Thus, Applicants have not provided sufficient guidance to make such.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including an isolated nucleic acid molecule of SEQ ID NO 20 comprising *crtE, idi, crtX, crtY, crtI, crtB,* and *crtZ* genes or an isolated nucleic acid molecule having at least 95% identity to SEQ ID NO 20, wherein said nucleic acid molecule encodes all of the polypeptides crtE, idi, crtX, crtY, crtI, crtB, and crtZ. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those nucleic acids having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Remarks

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, please contact the examiner's supervisor, Kathleen Kerr at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-9949.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Patent Examiner: Jae W. Lee, Ph.D.

RICHARD HUTSON, PH.D.
PRIMARY EXAMINER